

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
BRITISH AMERICAN TOBACCO R&D CENTRE
Patents Department
Attn. Drakeford, Robert W.
Regents Park Road
Southampton SO15 8TL
UNITED KINGDOM

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

DENN:

08/12/04

(PCT Rule 44.1)

Applicant's or agent's file reference

RD-ATC-32

Date of mailing
(day/month/year)

08/10/2004

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/GB2004/002583

International filing date
(day/month/year)

17/06/2004

Applicant

ADVANCED TECHNOLOGIES (CAMBRIDGE) LIMITED

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority

 European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stefanie Büchler

EV 331 383705 41

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference RD-ATC-32	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/GB2004/002583	International filing date (day/month/year) 17/06/2004	(Earliest) Priority Date (day/month/year) 17/06/2003
Applicant ADVANCED TECHNOLOGIES (CAMBRIDGE) LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☒ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regards to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. 1

☐ as suggested by the applicant.

☒ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB2004/002583

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01H5/00 C12N15/82 C12N15/29 C07K14/415 A23L1/0522

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MACGREGOR E A ET AL: "Structural models of limit dextrinase inhibitors from barley" JOURNAL OF CEREAL SCIENCE, vol. 31, no. 1, January 2000 (2000-01), pages 79-90, XP002297305 ISSN: 0733-5210	19-46
Y	page 80, left-hand column, line 17 - line 23 page 85, right-hand column, last paragraph; figure 1 page 88, right-hand column, line 9 - line 29 ----- -/-	1-18, 47-54

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

22 September 2004

Date of mailing of the international search report

08/10/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Loubradou, G

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LAZARO A ET AL: "SIGNAL PEPTIDE HOMOLOGY BETWEEN THE SWEET PROTEIN THAUMATIN II AND UNRELATED CEREAL ALPHA AMYLASE-TRYPSIN INHIBITORS" FEBS LETTERS, vol. 239, no. 1, 1988, pages 147-150, XP002297306 ISSN: 0014-5793 abstract; figure 1	19-46
Y	DINGES JASON R ET AL: "Mutational analysis of the pullulanase-type debranching enzyme of maize indicates multiple functions in starch metabolism." PLANT CELL, vol. 15, no. 3, March 2003 (2003-03), pages 666-680, XP002297307 ISSN: 1040-4651 the whole document	1-18, 47-54
Y	SLATTERY C J ET AL: "Engineering starch for increased quantity and quality" TRENDS IN PLANT SCIENCE, ELSEVIER SCIENCE, OXFORD, GB, vol. 5, no. 7, July 2000 (2000-07), pages 291-298, XP002241850 ISSN: 1360-1385 page 294, right-hand column, last paragraph; figure 1 page 296, left-hand column, paragraph 5	1-18, 47-54
Y	WO 98/50562 A (DU PONT ; BROGLIE KAREN E (US)) 12 November 1998 (1998-11-12) page 1, line 17 - line 24 page 1, line 37 - line 39 page 9, line 30 - line 33; example 3	1-18, 47-54
A	FUJITA NAOKO ET AL: "Antisense inhibition of isoamylase alters the structure of amylopectin and the physicochemical properties of starch in rice endosperm." PLANT AND CELL PHYSIOLOGY, vol. 44, no. 6, June 2003 (2003-06), pages 607-618, XP009036429 ISSN: 0032-0781 the whole document	

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>JAMES M G ET AL: "CHARACTERIZATION OF THE MAIZE GENE SUGARY1, A DETERMINANT OF STARCHCOMPOSITION IN KERNELS" PLANT CELL, AMERICAN SOCIETY OF PLANT PHYSIOLOGISTS, ROCKVILLE, MD, US, vol. 7, 1 April 1995 (1995-04-01), pages 417-429, XP002033602 ISSN: 1040-4651 the whole document</p> <p>-----</p>	
A	<p>WO 02/101059 A (BAYER CROPS SCIENCE GMBH) 19 December 2002 (2002-12-19) the whole document</p> <p>-----</p>	
A	<p>WO 03/014365 A (GEMSTAR CAMBRIDGE LTD) 20 February 2003 (2003-02-20) the whole document</p> <p>-----</p>	
A	<p>WO 03/035874 A (GEMSTAR CAMBRIDGE LTD) 1 May 2003 (2003-05-01) the whole document</p> <p>-----</p>	
P,A	<p>MACGREGOR E A: "The proteinaceous inhibitor of limit dextrinase in barley and malt" BIOCHIMICA ET BIOPHYSICA ACTA, vol. 1696, no. 2, 12 February 2004 (2004-02-12), pages 165-170, XP004489005 the whole document</p> <p>-----</p>	
T	<p>STAHL YVONNE ET AL: "Antisense downregulation of the barley limit dextrinase inhibitor modulates starch granule size distribution, starch composition and amylopectin structure." THE PLANT JOURNAL : FOR CELL AND MOLECULAR BIOLOGY. AUG 2004, vol. 39, no. 4, August 2004 (2004-08), pages 599-611, XP002297308 ISSN: 0960-7412 page 606, right-hand column, last paragraph - page 607, left-hand column, paragraph 2</p> <p>-----</p>	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB2004/002583

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9850562	A	12-11-1998	AU 7471798 A	27-11-1998
			BR 9815520 A	31-07-2001
			CA 2284688 A1	12-11-1998
			CN 1257544 T	21-06-2000
			EP 0981628 A1	01-03-2000
			HU 0001306 A2	28-09-2000
			ID 22673 A	09-12-1999
			WO 9850562 A1	12-11-1998
			US 6429358 B1	06-08-2002
WO 02101059	A	19-12-2002	CA 2465884 A1	19-12-2002
			WO 02101059 A2	19-12-2002
			US 2003126633 A1	03-07-2003
WO 03014365	A	20-02-2003	CA 2455200 A1	20-02-2003
			EP 1417322 A2	12-05-2004
			WO 03014365 A2	20-02-2003
			US 2003200564 A1	23-10-2003
WO 03035874	A	01-05-2003	CA 2463695 A1	01-05-2003
			EP 1440153 A1	28-07-2004
			WO 03035874 A1	01-05-2003
			US 2003177532 A1	18-09-2003

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/GB2004/002583

International filing date (day/month/year)
17.06.2004

Priority date (day/month/year)
17.06.2003

International Patent Classification (IPC) or both national classification and IPC
A01H5/00, C12N15/82, C12N15/29, C07K14/415, A23L1/0522

Applicant
ADVANCED TECHNOLOGIES (CAMBRIDGE) LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

10/561084
International application No.
PCT/GB2004/002583

IAP20 Rec'd PCT/PTO 16 DEC 2005

Box No. 1 Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed.
 - ☒ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002583

Box No. II Priority

1. ☒ The following document has not been furnished:
- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).
- Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18, 20, 22, 24, 27-54
	No: Claims	19, 21, 23, 25, 26
Inventive step (IS)	Yes: Claims	
	No: Claims	1-54
Industrial applicability (IA)	Yes: Claims	1-54
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)
and / or
2. Non-written disclosures (Rules 43*bis*.1 and 70.9)
see form 210

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/002583

IAP20 REPLY TO 16 DEC 2005

Reference is made to the following documents:

- D1: LAZARO A ET AL: "SIGNAL PEPTIDE HOMOLOGY BETWEEN THE SWEET PROTEIN THAUMATIN II AND UNRELATED CEREAL ALPHA AMYLASE-TRYPSIN INHIBITORS" FEBS LETTERS, vol. 239, no. 1, 1988, pages 147-150, XP002297306 ISSN: 0014-5793
- D2: MACGREGOR E A ET AL: "Structural models of limit dextrinase inhibitors from barley" JOURNAL OF CEREAL SCIENCE, vol. 31, no. 1, January 2000 (2000-01), pages 79-90, XP002297305 ISSN: 0733-5210
- D3: DINGES JASON R ET AL: "Mutational analysis of the pullulanase-type debranching enzyme of maize indicates multiple functions in starch metabolism." PLANT CELL, vol. 15, no. 3, March 2003 (2003-03), pages 666-680, XP002297307 ISSN: 1040-4651
- D4: SLATTERY C J ET AL: "Engineering starch for increased quantity and quality" TRENDS IN PLANT SCIENCE, ELSEVIER SCIENCE, OXFORD, GB, vol. 5, no. 7, July 2000 (2000-07), pages 291-298, XP002241850 ISSN: 1360-1385
- D5: WO 98/50562 A (DU PONT ; BROGLIE KAREN E (US)) 12 November 1998 (1998-11-12)

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1- D1 discloses the nucleotide and polypeptide sequence of the limit dextrinase inhibitor from barley (see Figure 1 of D1). The polypeptide sequence of D1 differs at 2 positions from the sequence of SEQ ID N°2 of the present application (98,6% of identity) and the nucleotide sequence of D1 shares 99% identity with the sequence of SEQ ID N°1 of the present application. The polynucleotide of D1 is inherently cloned in a vector having a selectable marker gene. Therefore, claims 19 and 21, 23, 25 and 26 are not novel (Article 33.2 PCT).
- 2- D2 discloses the sequences of the low and high pI inhibitors from barley (Figure 1 of D2). Said sequences are comprised in the sequence of SEQ ID N°2. Therefore, claim 22 is not novel (Article 33.2 PCT). In addition, the disclosure of the sequence of a polypeptide is inherently a

disclosure of the sequence of the polynucleotide encoding said polypeptide. As a consequence, said polynucleotide cannot involve an inventive step.
Therefore, claim 20 does not involve an inventive step (Article 33.3 PCT).

3- The subject-matter of claims 24, 27, 28 and 29 is immediately derivable from the subject-matter of D1 or D2 and therefore cannot involve an inventive step (Article 33.3 PCT).

4.1 The polypeptides of D1 and D2 are clearly identified in D2 as limit dextrinase inhibitors (see D2, the abstract and page 88 right-hand column last paragraph). D2 further indicates that the inhibitors are important for the malting and brewing industries (page 80 left-hand column, lines 17 to 23) and that a reduction in the activity of said inhibitors should lead to a greater fermentability.
Therefore, there is a motivation in the art to generate plants having a reduced level of limit dextrinase inhibitor activity. An obvious solution is to generate transgenic plant wherein the expression of the limit dextrinase inhibitor is down regulated, for example by using the anti-sense technology.
In addition, it can be noted that the plants obtained by the method of claims 1-18 are not different from plants transformed with an anti-sense construct down-regulating the expression of the barley limit dextrinase inhibitor.
Therefore, claims 30 to 33 and 42 to 46 do not involve an inventive step (Article 33.3 PCT).

4.2 The applicant is also invited to note that there is a general motivation in the art to alter/understand starch metabolism in plants and that one of the target is limit dextrinase (pullulanase) (see for example: D3, the abstract; D4 the abstract, page 294 right-hand column the last paragraph and page 296 left-hand column, the paragraph entitled "Starch debranching enzymes"; D5 page 1 lines 17 to 22 and lines 37 to 39). It is obvious for the skilled person that modifying the expression of the limit dextrinase inhibitor (overexpression or down regulation) will result in modifications in the limit dextrinase activity. Therefore, plants overexpressing the limit dextrinase inhibitor are also considered as lacking an inventive step.
The plants of claims 34 to 41 are apparently **inherently** obtained following either down regulation or overexpression of the limit dextrinase inhibitor, therefore said plants cannot involve an inventive step (Article 33.3 PCT).
The objection applies *mutatis mutandis* to the starch of claims 48 to 54.

5. It is obvious for the skilled person facing the problem of obtaining a plant having an altered ability to degrade starch that any modification of a gene involved in starch degradation will solve the problem. It is well known in the art that limit dextrinase is involved in starch degradation and that the limit dextrinase inhibitor regulates the activity of limit dextrinase (see for example D2 and D3). Therefore, the solution consisting in altering the expression of the limit dextrinase inhibitor in order to modify the activity of limit dextrinase is considered obvious.
Therefore, claim 3 does not involve an inventive activity (Article 33.3 PCT).
Dependent claims 4 to 18 do not appear to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.
6. The attention of the applicant is drawn to the fact that the modification mentioned in claims 1 and 2 are not limited to the specific starch granules modifications observed in the examples but are drafted in a very broad way. The following objection is based on this fact.
The method of claim 1 is not directed to a specific modification of the starch granule and the method of claim 2 defines de modification so broadly that they cover most of the possible modifications.
Facing the problem of modifying starch granules in general, it is obvious for the skilled person that modifying the activity of any gene involved in starch metabolism would be suitable. The barley limit dextrinase inhibitor is known to regulate the activity of the limit dextrinase which plays an important role both in starch synthesis and starch degradation. Therefore, It is obvious for the skilled person that modifying the expression of the limit dextrinase inhibitor will lead to starch granule modification *via* the inhibition or lack of inhibition of the limit dextrinase. Therefore, claims 1 and 2 are not considered to involve an inventive activity (Article 33.3 PCT).
7. Claims 1 to 54 meet the requirements of Article 33.4 PCT.